REMARKS

I. Remarks and Amendments

The Applicants' agents would like to thank Examiners Cherie Woodward and Brenda Brumback for taking the time on February 17, 2006 to discuss the instant application and issues raised in the previous Office Actions of record. The Applicants' agents would also like to thank Examiners Cherie Woodward and Marianne Allen for their time on October 4, 2006 in discussing the application and the Advisory Action.

Claims 1-12, 14, and 17-19 are currently pending and are under examination. Claim 8 has been withdrawn from consideration. Claims 13, 15, and 16 were previously canceled. Claim 19 is canceled herein. Claims 1, 5, 9, and 10 are amended herein.

Claims 1, 9, and 10 are amended to recite that the claimed methods involve "administering an effective amount of a composition comprising Granulocyte Colony Stimulating Factor (G-CSF) polypeptide after but not before AMI."

Claim 5 is amended to include reference to individual species of interleukins and remove reference to a genus of interleukins.

Claim 10 is also amended to remove the words "and prevent" solely in order to expedite prosecution.

No new matter is introduced by the amendment to the claims. Support for the amendments is found throughout the specification and the original claims as filed. The Applicants do not intend, with these or any other amendments, to abandon the subject matter of claims previously presented, and reserve the right to pursue such subject matter in duly filed continuing patent applications.

The Applicants respectfully request entry of the present amendment.

II. Patentability Arguments

A. The Rejections under 35 U.S.C. § 102(b) May Properly Be Withdrawn.

1. Orlic and Orlic as evidenced by Gottlieb do not anticipate the subject matter of any pending claim.

The Examiner maintained the rejection of claims 1, 2, and 9 under 35 U.S.C. § 102(b) for anticipation by Orlic et al., *Proc. Natl. Acad. Sci.* 98:10344-10349, 2001 (hereinafter "Orlic"). Orlic assertedly discloses the administration of a composition comprising G-CSF three days following coronary artery ligation, in addition to five days preceding coronary artery ligation, demonstrating that this composition was given following ischemia and not merely prophylactically. The Examiner acknowledged in the telephonic interview of February 17, 2006 and in the Office Action at page 6 that Orlic teaches the administration of a composition comprising G-CSF both before and after AMI. However, the Examiner asserted that the additional steps taught by Orlic are not limiting as applied to the instant claims, because as long as Orlic teaches the steps of the instant claimed methods the disclosure anticipates the claimed methods. Office Action at page 6.

While the Applicants disagree with the Examiner for the reasons provided in the prior responses of record, the Applicants have amended claim 1 to replace the phrase "administering an effective amount of a composition comprising Granulocyte Colony Stimulating Factor (G-CSF) polypeptide after AMI" with "administering an effective amount of a composition comprising Granulocyte Colony Stimulating Factor (G-CSF) polypeptide after but not before AMI" and claim 9 to replace the phrase " administering an effective amount of a composition comprising Granulocyte Colony Stimulating Factor (G-CSF) polypeptide after occlusion in an artery" with " administering an effective amount of a composition comprising Granulocyte Colony Stimulating Factor (G-CSF) polypeptide after but not before occlusion in an artery" solely in order to expedite prosecution. Thus, Orlic does not disclose each element of independent claims 1 and 9, as amended.

As a matter of law, a dependent claim incorporates each limitation of a claim from which it depends. 35 U.S.C. § 112, fourth paragraph. Claim 2 depends from claim 1 and, as established above, Orlic does not disclose each element of claim 1, as amended. Accordingly, Orlic cannot and does not disclose, expressly or inherently, each limitation of dependent claim 2 and, for that reason, the rejection of claims 1, 2, and 9 under 35 U.S.C. §

102(b) for anticipation by Orlic is rendered moot by the amendments to claims 1 and 9 herein.

The Examiner also maintained the rejection of claims 11, 12, 14, and 16 and rejected new claims 17 and 18 under 35 U.S.C. §102(b) as assertedly being anticipated by Orlic as evidenced by Gottlieb et al. (*Ann. N.Y. Acad. Sci.* 874: 412-426, 1999; hereinafter "Gottlieb") for reasons of record and for reasons set out in the instant Office Action at pages 7-8. In the Office Action mailed November 14, 2005, the Examiner reasoned that the claims recite improvements in a method of reperfusion therapy where the reduction in damage is characterized by improvement in cardiac function, reduced scarring of the myocardium, reduction in cardiomyocyte apoptosis, reduction in necrosis, regeneration of the myocardium, and neoangiogenesis in the infarct zone. The Examiner asserted that Orlic discloses an improvement in cardiac function of mice after infarct-related myocardial tissue damage and treatment with G-CSF, myocardial regeneration after infarct-related myocardial tissue damage and treatment with G-CSF, reduced scarring of the myocardium after treatment with G-CSF, and neoangiogenesis in the infarcted zone after infarct-related myocardial tissue damage and treatment with G-CSF. Gottlieb was cited for assertedly disclosing that necrosis and apoptosis are inherent properties of scarring resulting from cardiac infarction.

While the Applicants disagree with the Examiner for the reason provided in the prior response of record, the amendment to claim 1, from which all claims 11, 12, 14, (claim 16 was canceled in the previous amendment), 17, and 18 depend renders moot the rejection of claim 1 as being anticipated by Orlic. Thus, because the disclosure of Orlic cannot anticipate the subject matter of claim 1 as amended, Orlic as evidenced by Gottlieb cannot possibly anticipate claims 11, 12, 14, 17, and 18 which depend from claim 1 for the reasons set out above. Therefore, the disclosure of Gottlieb has no relevance and the rejection under 35 U.S.C. § 102(b) is rendered moot by the amendment to clam 1 herein and should be withdrawn.

2. Anversa and Anversa as evidenced by Gottlieb do not anticipate the subject matter of any pending claim.

The Examiner maintained the rejection of claims 1-7 and 9-10 under 35 U.S.C. § 102(b) as assertedly anticipated by the disclosure of Anversa, (Pre-grant Patent

Publication No. US 2002/0061587 A1 [05/2002]; hereinafter "Anversa") for reasons of record in the Office Actions of March 22, 2005 and October 20, 2004. The Examiner also asserted that: 1) Anversa discloses the administration of cytokines, including G-CSF, for the treatment of infarct-related myocardial tissue damage (page 1, paragraph [006]); 2) Anversa's methods to restore cardiac function take advantage of the regenerative properties of stem cells and cytokines (page 1, paragraph [0003]; and page 2, paragraph [0022], respectively); 3) Anversa's methods are also drawn to treating cardiovascular diseases, including ischemia, and define ischemic events as encompassing clinical scenarios such as bypass surgery (page 1, paragraph [0003]; and page 2, paragraph [0014], respectively); and 4) Anversa stated that the administration of cytokines, including G-CSF, following ischemia involves neoangiogenesis and restores "structural and functional integrity to the infarcted area" (page 3, paragraph [0038]; and page 4, paragraph [0044]). The Examiner asserted that as long as Anversa teaches each of the steps of the instant claimed methods, Anversa's teachings fully encompass the claimed methods. The Examiner acknowledged in the telephonic interview of February 17, 2006 and in the Office Action at pages 6-7 that Anversa teaches the administration of a composition comprising G-CSF both before and after AMI; however, the Examiner asserted that the additional steps taught by Anversa, like Orlic as set out above, are not limiting as applied to the instant claims, because as long as Anversa teaches each of the steps of the instant claimed methods their disclosure anticipates the claimed methods herein. Office Action at pages 6-7.

While the Applicants disagree with the Examiner for the reasons provided in the prior responses of record, the Applicants have amended claim 1 to replace the phrase "administering an effective amount of a composition comprising Granulocyte Colony Stimulating Factor (G-CSF) polypeptide after AMI" with "administering an effective amount of a composition comprising Granulocyte Colony Stimulating Factor (G-CSF) polypeptide after but not before AMI". The Applicants have also amended claims 9 and 10 to replace the phrases " administering an effective amount of a composition comprising Granulocyte Colony Stimulating Factor (G-CSF) polypeptide after occlusion in an artery" with " administering an effective amount of a composition comprising Granulocyte Colony Stimulating Factor (G-CSF) polypeptide after but not before occlusion in an artery". These amendments have been made solely in order to expedite prosecution.

The Examiner has also maintained that Anversa, at paragraphs [0037] and [0038], teaches administration of a cytokine following MI (*see* Interview Summary mailed October 11, 2006), thereby assertedly anticipating the subject matter of the claims. The Applicants respectfully disagree.

In paragraph [0037], Anversa discusses results of an experiment, presumably summarizing the results of Example 1 (*see* Anversa at pages 13-14), wherein the authors harvested mouse stem cells, induced an MI, and then, via surgery, injected stem cells back into the mouse heart to look at their restorative function (*see* Anversa, Example 1, at pages 13-14). If true, Anversa, in Example 1, is clearly not administering a cytokine post-MI and, therefore, not anticipating the claimed subject matter.

In paragraph [0038], Anversa states that "***it has surprisingly been found*** that following a myocardial infarction, the administration of a cytokine to the patient, stimulates the patient's own stem cells them to enter the blood stream and home to the infarcted area. It has also been found that once cells home to the infarct . . . restoring structural and functional integrity to the infracted [sic] area." (emphasis added.) Because Anversa is discussing what has "surprisingly been found," i.e. in the past tense, we look at experiments already performed in the Anversa application in order to determine how, or in this case if, these surprising results were observed. By reviewing the Anversa application, the Applicants presume that Anversa in paragraph [0038] is discussing the results of experiments presented in Example 2 (*see* Anversa at pages 14-16), because only in Example 2 did the authors administer cytokines *in vivo* to stimulate the patient's own stem cells to home to the infarct. However, in Example 2 the authors followed a protocol of cytokine treatment wherein both SCF and G-CSF were administered five days before MI and then for another 3 days following MI.

Unless Anversa is relying on data not disclosed in their application, Anversa's Examples are inconsistent with what "**has surprisingly been found**" as mentioned in paragraph [0038]. What Anversa did was not **only** a post-infarction treatment as the Applicants are claiming. Instead, Anversa carried out both a pre- and post-infarction treatment with cytokines. Thus, there was no scientific data to show that treatment with G-CSF alone after, but not before, AMI would have any "**surprising**" effect on patient therapy.

As the Patent Office requires, "no results should be represented as actual results unless they have actually been achieved." M.P.E.P. § 608.01(p). Paper examples should not be described using the past tense. *Hoffman-La Roche, Inc. v. Promega Corp.*, 323 F.3d 1354, 1367 (Fed. Cir. 2003). Absent some other data that Anversa did not disclose, the Examiner is therefore relying on an unsubstantiated statement in Anversa that is simply not demonstrated and, therefore, not enabled, because such results have not actually been achieved.

Consequently, the rejection of claims 1, 9, and 10 under 35 U.S.C. § 102(b) for anticipation by Anversa is rendered moot-in-part by the amendments herein to claims 1, 9, and 10 and overcome-in-part by the remarks provided above.

As set out above in II(A)(1), it is a matter of law that a dependent claim incorporates each limitation of a claim from which it depends. 35 U.S.C. § 112, fourth paragraph. Each of claims 2-7 depend from claim 1 and, as established above, Anversa does not disclose each element of claim 1, as amended. Accordingly, Anversa cannot and does not disclose, expressly or inherently, each limitation of dependent claims 2-7 and, for that reason, the rejection of claims 1, 2-7, and 9-10 under 35 U.S.C. § 102(b) for anticipation by Anversa is rendered moot by the amendments to claims 1, 9, and 10 herein.

The Examiner also maintained the rejection of claims 11, 12, 14, and 16 and rejected new claims 17 and 18 under 35 U.S.C. § 102(b) as assertedly being anticipated by Anversa as evidenced by Gottlieb for reasons of record and for reasons set out in the instant Office Action at pages 8-9. In the Office Action mailed November 14, 2005, the Examiner reasoned that the claims recite improvements in a method of reperfusion therapy where the reduction in damage is characterized by improvement in cardiac function, reduced scarring of the myocardium, reduction in cardiomyocyte apoptosis, reduction in necrosis, regeneration of the myocardium, and neoangiogenesis in the infarct zone. The Examiner also asserted that 1) Anversa discloses that the administration of cytokines, including G-CSF, for the treatment of myocardial tissue damage; 2) the methods of Anversa are drawn to treating cardiovascular diseases, including ischemia, and the methods take advantage of the regenerative properties of stem cells and cytokines; and 3) the administration of cytokines following ischemia involves neoangiogenesis. Moreover, Anversa assertedly discusses myocardial regeneration and reduced scar formation in cytokine-treated mice. Gottlieb was cited for assertedly

disclosing that necrosis and apoptosis are inherent properties of scarring resulting from cardiac infarction.

While the Applicants disagree with the Examiner for the reason provided in the prior response of record, the amendment to claim 1 herein, from which all claims 11, 12, 14, (claim 16 was canceled in the previous amendment), and 17-19 depend, renders moot the rejection of claim 1 as being anticipated by Anversa. Therefore, because the disclosure of Anversa, like the disclosure of Orlic discussed above, cannot anticipate the subject matter of claim 1 as amended, Anversa as evidenced by Gottlieb cannot possibly anticipate claims 11, 12, 14, and 17-18 (claim 19 is canceled herein) which depend from claim 1 for the reasons set out above. Therefore, the disclosure of Gottlieb has no relevance and the rejection under 35 U.S.C. § 102(b) is rendered moot by the amendment to clam 1 herein and should be withdrawn.

B. The Enablement Rejection Under 35 U.S.C. §112, First Paragraph, May Properly Be Withdrawn.

The Examiner maintained the rejection of claim 5 for lack of enablement for assertedly not fully enabling the administration of interleukins because IL-8 is a species of interleukin that is included in the genus of "interleukins" recited in claim 5. Office Action at pages 3-4. The administration of IL-8 was rejected previously by the Examiner for reasons of record.

While the Applicants disagree with the Examiner for the reasons provided in the prior responses of record, the Applicants have amended claim 5 to remove reference to the genus "interleukins" solely in order to expedite prosecution. Thus, the amendment to claim 5 herein renders moot the rejection of claim 5 for lack of enablement.

Further, claim 10 was rejected for an asserted lack of enablement for the prevention of tissue damage. The examiner has asserted that prevention involves underlying the cause of the tissue damage, i.e., disrupting the mechanisms which give rise to the tissue damage *a priori*, and the causes of tissue damage in occluded arteries are multifactorial. Office Action at pages 9-10.

In response, the Applicants respectfully disagree, however, in order to expedite prosecution, the Applicants have amended claim 10 to remove the word "prevent" from the claim. Consequently, the rejection of claim 10 for lack of enablement is rendered moot by amendment.

In view of the foregoing comments and the amendments to the claims, the Applicants submit that claims 5 and 10 are fully enabled by the specification and the rejection of these claims under 35 U.S.C. § 112, first paragraph, has been rendered moot.

C. The Rejection Under 35 U.S.C. § 112, Second Paragraph, May Properly Be Withdrawn.

The Examiner rejected claims 1-7, 9, and 11-16 under 35 U.S.C. §112, second paragraph, for failing to point out and distinctly claim the subject matter of the invention. The rejection was based on the methods being drawn to "administration before, concurrently with, and/or after reperfusion therapy," which assertedly renders the claims indefinite, because it extends the method outside the reperfusion therapy. The Examiner's rejection is based on an asserted lack of limits in the claims or specification such that one would know how long before reperfusion therapy one should administer G-CSF, and the claims read on the administration as being at any time before or after reperfusion therapy. The Examiner also rejected claim 10 under 35 U.S.C. §112, second paragraph, because the phrase "administration before, concurrently with, and/or after bypass surgery" assertedly renders the claim indefinite for extending the method outside of the bypass surgery. Like the rejection of claims 1-7, 9, and 11-16 recited *supra*, the Examiner has asserted that the lack of a defined time period for the administration of G-CSF is rendering claim 10 indefinite as well. Office Action at pages 4-5. In response, the Applicants respectfully traverse the rejections.

> "The requirement to "distinctly" claim means that the claim must have a meaning discernible to one of ordinary skill in the art when construed according to correct principles." *Union Pac. Res. Co. v. Chesapeake Energy Corp.*, 236 F.3d 684, 692 (Fed. Cir. 2001).

The Applicants submit that the rejected claims, as amended, satisfy the above-recited requirement. Independent claim 1, from which claims 2-7 and 11-14 depend (claims 15 and 16 were canceled in the previously filed amendment), is amended herein to recite that

G-CSF may be administered "after but not before AMI, but before, concurrently with, and/or after reperfusion therapy." Independent claim 9 is amended herein to recite "after but not before occlusion in an artery, but before, concurrently with, and/or after reperfusion therapy." As well, independent claim 10 is amended herein to recite " after but not before occlusion in an artery, but before, concurrently with, and/or after bypass surgery."

Further, the Applicants submit that there is not a lack of a defined time period in these claims and one of skill in the art, in view of the claims and the specification, could determine when G-CSF administration is beneficial to patient outcome. For example, the specification discusses that G-CSF treatment is given in conjunction with reperfusion therapy (*see* specification at least at page 1, lines 4-8; at page 3, lines 4-8; at page 5, lines 23-25 and 29-30; at page 8, lines 2-4; and at page 9, lines 20-22). The specification contemplates, at least at page 11, lines 3-7, that these methods of therapy may be administered in multiple administrations "simultaneously or may be administered over a period of several hours. In certain cases, it may be beneficial to provide a continuous flow of the therapeutic composition. Additional therapy may be administered on a period basis, for example, daily, weekly, or monthly."

The specification also provides examples (*see* Examples 1 and 2 at pages 19-21) of administering G-CSF immediately at the onset of AMI, after reperfusion at various time intervals, and sometimes extending to at least 20 days post-AMI. Moreover, Example 2 provides an example of determining the critical time period for G-CSF administration after AMI. Consequently, the specification provides guidance so that one of skill in the art can determine the critical time period, and also determine the time period for which treatment with G-CSF after AMI in conjunction with reperfusion therapy remains beneficial to a patient.

Although it is indeed possible that "a cancer patient who receives G-CSF treatment 48 hours after receiving reperfusion therapy would fall within the claimed method (*see* Office Action at page 5), " the Applicants respectfully disagree that this use of G-CSF is relevant to the claimed subject matter. There are many compounds that are known to have multiple treatment applications in the medical field, and the use of G-CSF to treat cancer patients does not preclude the patentability of methods of using G-CSF in conjunction with reperfusion to improve patient outcome. Moreover, when a physician is interested in saving

the life or improving the outcome of a patient who has just undergone an AMI, the patient's cancer therapy becomes a secondary consideration to the primary consideration of treating the patient to survive the AMI with minimal damage to the cardiovascular system.

Moreover, independent claims 1, 9, and 10 all recite that the claimed subject matter is directed to an "improvement" in a " reperfusion therapy method" or a "bypass surgery method" (another means of reperfusion therapy) where a composition comprising Granulocyte Colony Stimulating Factor (G-CSF) polypeptide is administered. Thus, the claimed subject matter, as amended, allows for the administration of G-CSF in a reperfusion therapy method **after but not before AMI, but before, concurrently with, and/or after reperfusion therapy** for the time period necessary to obtain a beneficial outcome. One of skill in the art will be able to apply this method within these parameters. Consequently, one skilled in the art will know that G-CSF administration must be administered within an effective time frame after an AMI or after occlusion in an artery to be effective. The claims already provide that G-CSF administration is "after" an ischemic event. Accordingly, the skilled artisan can determine how long after the event such a treatment will provide benefit to the patient.

In view of the discussion provided above, the Applicants respectfully submit that the rejection of claims 1-7 and 9-14 under 35 U.S.C. § 112, second paragraph, has been overcome and should be withdrawn.

III. Conclusion

In view of the above, the Applicants respectfully submit that the claims are in condition for allowance and respectfully request expedited notification of same. Should the Examiner have any questions, she is welcomed to contact the undersigned at the telephone number below.

Respectfully submitted,

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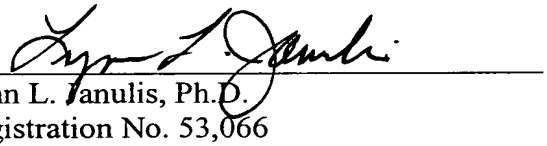
By: 

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